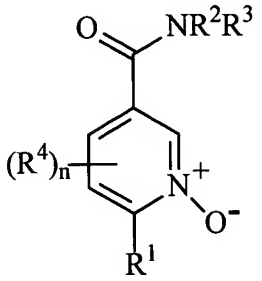
CLAIMS

1. A compound having the structure (I):



(I)

and optical isomers, diastereomers, enantiomers and pharmaceutically acceptable salts thereof, wherein

R^1 is selected from R^5 and R^5-(C_1-C_6heteroalkylene)- where R^5 is selected from hydrogen, halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring, amino or hydroxy;

R^2 and R^3 are independently hydrogen, alkyl, heteroalkyl, aryl, aryl(akylene), heteroaryl, heteroaryl(alkylene), carbocycle, carbocycle(alkylene), heterocycle, and heterocycle(alkylene);

each occurrence of R^4 is independently selected from halogen, alkyl, heteroalkyl, aryl, heteroaryl, carbocycle aliphatic ring and heterocycle aliphatic ring, amino or hydroxy; and

n is 0, 1, 2 or 3.

2. A compound of claim 1 wherein n is 0.

3. A compound of claim 1 wherein n is 1.

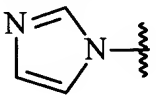
4. A compound of claim 1 wherein n is 0 or 1 and R^2 is H.

5. A compound of claim 4 wherein R^1 is R^5-SO_2- and R^5 is selected from alkyl, heteroalkyl, aryl, carbocycle, aryl(alkylene), and carbocycle(alkylene).

6. A compound of claim 5 wherein, for R^5, alkyl is C_1-C_{10}alkyl; heteroalkyl is C_1-C_{10}alkyl with 1, 2 or 3 heteroatoms selected from N, O and S; aryl is phenyl, substituted phenyl, naphthyl or substituted naphthyl; carbocycle is C_3-C_8carbocycle; and alkylene is C_1-C_{10}alkylene.

7. A compound of claim 5 wherein R^1 is selected from (C_1-C_6alkyl)SO_2-, $PhSO_2$-, fluorinatedphenylSO_2-, $PhCH_2SO_2$-, cyclopentylSO_2-, *m*-carboxyphenylSO_2-, *m*-methylphenylSO_2-, and HOOC-(C_1-C_4alkylene)SO_2-.

8. A compound of claim 1 wherein R^1 is selected from halogen, amino, hydrocarbylamino, dihydrocarbylamino, hydrocarbyloxy, hydrocarbylthio, heterocyclyl, (heteroalkyl)amino, and (heteroaryl)amino.

9. A compound of claim 7 wherein R^1 is selected from amino, (C_1-C_6alkyl)(C_1-C_6alkyl)amino, PhNH-, $PhCH_2NH$-,  , and $HOCH_2CH_2NH$-.

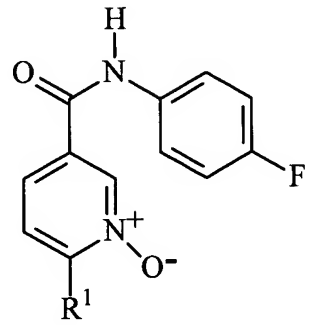
10. A compound of claim 8 wherein R^1 is selected from halide and (C_1-C_6alkyl)S-.

11. A compound of claim 10 wherein R^1 is chloride.

12. A compound of claim 4 wherein R^3 is selected from aryl, aryl(alkylene), heteroaryl, and heteroaryl(alkylene).

13. A compound of claim 12 wherein R^3 is aryl.

14. A compound of claim 1 having structure (II)



(II).

15. A compound of claim 14 wherein R^1 is selected from $(C_{1\text{-}6}alkyl)SO_2$-, $PhSO_2$-, fluorinatedphenylSO_2-, $PhCH_2SO_2$-, cyclopentylSO_2-, *m*-carboxyphenylSO_2-, *m*-methylphenylSO_2-, and HOOC-(C_1-C_4alkylene)SO_2-.

16. A compound of claim 4 wherein R^3 is benzyl or phenyl, the benzyl or phenyl having 0, 1, 2, 3 or 4 substituents selected from alkoxy, alkoxycarbonyl, alkyl, alkylamido, alkylcarbonyl, amido, benzyl optionally substituted with halogen, benzyloxy, carboxy, cyano, dialkylamido, haloalkyl, haloalkyloxy, halogen, hydroxy, nitro, oxoalkyl, phenyl optionally substituted with halogen, thioalkyl, thiocyanate, and thiohaloalkyl.

17. A compound of claim 1 wherein R^3 is selected from cycloalkyl, cycloalkyl(alkylene), cycloalkyl(heteroalkylene), heterocycloalkyl, heterocycloalkyl(alkylene), heterocycloalkyl(heteroalkylene), heteroaryl, heteroaryl(alkylene), and heteroaryl(heteroalkylene).

18. A compound of claim 1 wherein said compound is 6-Chloro-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.

19. A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-6-(2-hydroxy-ethylamino)-1-oxy-nicotinamide.

20. A compound of claim 1 wherein said compound is 6-Bromo-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.

21. A compound of claim 1 wherein said compound is 5,6-Dichloro-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.

22. A compound of claim 1 wherein said compound is 6-Ethanesulfonyl-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.

23. A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-1-oxy-6-(propane-2-sulfonyl)-nicotinamide.

24. A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-6-methanesulfonyl-1-oxy-nicotinamide.

25. A compound of claim 1 wherein said compound is 6-Benzenesulfonyl-N-(4-fluoro-phenyl)-1-oxy-nicotinamide.

26. A compound of claim 1 wherein said compound is N-(4-Fluoro-phenyl)-1-oxy-6-phenylmethanesulfonyl-nicotinamide.

27. A compound of claim 1 wherein said compound is 6-Chloro-N-(3-chloro-4-fluoro-phenyl)-1-oxy-nicotinamide.

28. A compound of claim 1 wherein said compound is 6-Chloro-N-(4-iodo-phenyl)-1-oxy-nicotinamide.

29. A compound of claim 1 wherein R^1 is selected from halogen, heteroalkyl or amino, R^2 is H, R^3 is aryl and R^4 is H.

30. A composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier, adjuvant or incipient.

31. A method for antagonizing chemokine receptors comprising administering to a patient in need thereof an effective amount of a compound of claim 1.

32. A method for inhibiting a chemokine-mediated cellular event comprising administering to a patient in need thereof an effective amount of a compound of claim 1.

33. A method of claim 32 wherein the compound inhibits IL-8 and or GRO-α driven neutrophil chemotaxis.

34. The method of claim 32 wherein the compound inhibits a CXCR1 receptor.

35. The method of claim 32 wherein the compound inhibits a CXCR2 receptor.

36. The method of claim 32 for the treatment of a disorder selected from Inflammatory Bowel Disease (IBD), psoriasis, rheumatoid arthritis, Acute Respiratory Distress Syndrome (ARDS), cancer, atherosclerosis, reperfusion injury, and graft vs. host disease.

37. A method for inhibiting a G-protein-coupled, seven-transmembrane domain (7TM) receptor in a patient comprising administering to the patient a compound of claim 1 in an amount effective to inhibit the receptor.

38. A method of claim 37 wherein the compound modulates the binding of Peptide YY (PYY) to a NPY cell receptor.

39. A method of claim 37 wherein the compound modulates the binding of somatostatin to a somatostatin cell receptor.

40. A method of claim 37 wherein the compound modulates the binding of MIP-1β to a CCR5 cell receptor.

41. A method for treating an inflammation event, comprising administering to a patient in need thereof, through a therapeutically or prophylactically acceptable manner, a therapeutically or pharmaceutically effective amount of the compound of claim 1.

42. The method of claim 41 wherein administration is selected from transdermal, oral, intravenous, intramuscular, vaginal, rectal, pulmonary, subcutaneous, sublingual and transmucosal administration.

43. A method for identifying a binding partner to a compound of claim 1 comprising:

immoblizing proteins known to be involved in the TNF-α signaling pathway onto a suitable carrier; and

passing a solution of said compounds in isolation or mixture over said proteins and analyzing for compound:protein complex formation using surface plasmon resonance (SPR).

44. A method for identifying a binding partner to a compound of claim 1 comprising:

providing said compound(s) bound to a solid support to provide solid phase compounds;

contacting a cell or cell components with said solid phase compounds in isolation or mixture;

removing uncomplexed cellular material, for example by gentle washing with aqueous buffer; and

recovering said binding partner from the solid phase compounds.